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<p>(21) International Application Number: PCT/US00/05882</p> <p>(22) International Filing Date: 8 March 2000 (08.03.00)</p> <p>(30) Priority Data: 60/124,270 12 March 1999 (12.03.99) US</p> <p>(71) Applicant (for all designated States except US): HUMAN GENOME SCIENCES, INC. [US/US]; 9410 Key West Avenue, Rockville, MD 20850 (US).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): ROSEN, Craig, A. [US/US]; 22400 Rolling Hill Road, Laytonsville, MD 20882 (US). RUBEN, Steven, M. [US/US]; 18528 Heritage Hills Drive, Laytonsville, MD 20882 (US).</p> <p>(74) Agents: WALES, Michele, M. et al.; Human Genome Sciences, Inc., 9410 Key West Avenue, Rockville, MD 20850 (US).</p>	<p>(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).</p> <p><b>Published</b> <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p>	
<p>(54) Title: HUMAN CANCER ASSOCIATED GENE SEQUENCES AND POLYPEPTIDES</p>		
<p>(57) Abstract</p> <p>This invention relates to newly identified tissue specific cancer associated polynucleotides and the polypeptides encoded by these polynucleotides herein collectively known as "cancer antigens", and to the complete gene sequences associated therewith and to the expression products thereof, as well as the use of such tissue specific cancer antigens for detection, prevention and treatment of tissue specific disorders, particularly the presence of cancer. This invention relates to the cancer antigens as well as vectors, host cells, antibodies directed to cancer antigens and recombinant and synthetic methods for producing the same. Also provided are diagnostic methods for diagnosing and treating, preventing and/or prognosing tissue specific disorders, including cancer, and therapeutic methods for treating such disorders. The invention further relates to screening methods for identifying agonists and antagonists of cancer antigens of the invention. The present invention further relates to methods and/or compositions for inhibiting the production and/or function of the polypeptides of the present invention.</p>		

*What Is Claimed Is:*

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:
- 5 (a) a polynucleotide fragment of SEQ ID NO:X or a polynucleotide fragment of the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- (b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:Y or a polypeptide fragment encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- 10 (c) a polynucleotide encoding a polypeptide fragment of a polypeptide encoded by SEQ ID NO:X or a polypeptide fragment encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- 15 (d) a polynucleotide encoding a polypeptide domain of SEQ ID NO:Y or a polypeptide domain encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- (e) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:Y or a polypeptide epitope encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X;
- 20 (f) a polynucleotide encoding a polypeptide of SEQ ID NO:Y or the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X, having biological activity;
- (g) a polynucleotide which is a variant of SEQ ID NO:X;
- 25 (h) a polynucleotide which is an allelic variant of SEQ ID NO:X;
- (i) a polynucleotide which encodes a species homologue of the SEQ ID NO:Y;
- (j) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(i), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide
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sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a protein.

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3. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding the sequence identified as SEQ ID NO:Y or the polypeptide encoded by the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X.

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4. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises the entire nucleotide sequence of SEQ ID NO:X or the cDNA sequence included in the related cDNA clone, which is hybridizable to SEQ ID NO:X.

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5. The isolated nucleic acid molecule of claim 2, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

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6. The isolated nucleic acid molecule of claim 3, wherein the nucleotide sequence comprises sequential nucleotide deletions from either the C-terminus or the N-terminus.

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7. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.

8. A method of making a recombinant host cell comprising the isolated nucleic acid molecule of claim 1.

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9. A recombinant host cell produced by the method of claim 8.

10. The recombinant host cell of claim 9 comprising vector sequences.
11. An isolated polypeptide comprising an amino acid sequence at least  
5 95% identical to a sequence selected from the group consisting of:
- (a) a polypeptide fragment of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
  - (b) a polypeptide fragment of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone, having biological activity;
  - 10 (c) a polypeptide domain of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
  - (d) a polypeptide epitope of SEQ ID NO:Y or of the sequence encoded by the cDNA included in the related cDNA clone;
  - (e) a full length protein of SEQ ID NO:Y or of the sequence encoded by the  
15 cDNA included in the related cDNA clone;
  - (f) a variant of SEQ ID NO:Y;
  - (g) an allelic variant of SEQ ID NO:Y; or
  - (h) a species homologue of the SEQ ID NO:Y.
- 20 12. The isolated polypeptide of claim 11, wherein the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.
- 25 13. An isolated antibody that binds specifically to the isolated polypeptide of claim 11.
14. A recombinant host cell that expresses the isolated polypeptide of claim 11.
- 30 15. A method of making an isolated polypeptide comprising:

(a) culturing the recombinant host cell of claim 14 under conditions such that said polypeptide is expressed; and

(b) recovering said polypeptide.

5           16.    The polypeptide produced by claim 15.

17.    A method for preventing, treating, or ameliorating a medical condition, comprising administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 11 or the polynucleotide of claim 1.

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18.    A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

15           (b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

19.    A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

20           (a) determining the presence or amount of expression of the polypeptide of claim 11 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

25           20.    A method for identifying a binding partner to the polypeptide of claim 11 comprising:

(a) contacting the polypeptide of claim 11 with a binding partner; and

(b) determining whether the binding partner effects an activity of the polypeptide.

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21. The gene corresponding to the cDNA sequence of SEQ ID NO:Y.
22. A method of identifying an activity in a biological assay, wherein the method comprises:
- 5 (a) expressing SEQ ID NO:X in a cell;
- (b) isolating the supernatant;
- (c) detecting an activity in a biological assay; and
- (d) identifying the protein in the supernatant having the activity.
- 10 23. The product produced by the method of claim 20.

864

Gly Ile Ser His Ala Pro Asn Ala Val Lys Thr Ala Phe Tyr Leu Ala  
 145 150 155 160

Glu Phe Phe Val Asn Glu Ala Arg Lys Asn Asn His His Phe Lys Ser  
 165 170 175

Glu Ser Glu Glu Glu Lys Ala Leu Ile Tyr Gln Phe Ser Pro Ile Tyr  
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Thr Gly Asn Ile Ser Ser Phe Gln Gln Cys Tyr Ile Phe Asp  
 195 200 205

<210> 913

<211> 91

<212> PRT

<213> Homo sapiens

<400> 913

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 1 5 10 15

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 20 25 30

Asp Ser Val Pro Gly Thr Tyr Arg Lys Val Val Ala Ala Arg Ala Pro  
 35 40 45

Arg Lys Val Leu Gly Ser Ser Thr Ser Ala Thr Asn Ser Thr Ser Val  
 50 55 60

Ser Ser Arg Lys Glu His Val Leu Cys Asn Leu Ile Thr Gln Met Met  
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Lys Lys Asn Arg Thr Phe Ser Phe Ile Phe Glu  
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<212> PRT

<213> Homo sapiens

<220>

<221> SITE

<222> (132)

<223> Xaa equals any of the naturally occurring L-amino acids

<220>

1472

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100 105 110

&lt;210&gt; 1401

&lt;211&gt; 69

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 1401

Arg Arg Gln Val Gly Ala Ala Ala Val Ala Met Thr Arg Gly Asn Gln  
1 5 10 15

Arg Glu Leu Ala Arg Gln Lys Asn Met Lys Lys Gln Ser Asp Ser Val  
20 25 30

Lys Gly Lys Arg Arg Asp Asp Gly Leu Ser Ala Ala Ala Arg Lys Gln  
35 40 45

Arg Asp Ser Glu Ile Met Gln Gln Lys Gln Lys Lys Ala Asn Glu Lys  
50 55 60

Lys Glu Glu Pro Lys  
65

&lt;210&gt; 1402

&lt;211&gt; 177

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (6)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (162)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids

&lt;220&gt;

&lt;221&gt; SITE

&lt;222&gt; (166)

&lt;223&gt; Xaa equals any of the naturally occurring L-amino acids